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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,212	06/07/2002	Atsushi Miyamoto	Q68293	4780

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/048,212	Applicant(s) MIYAMOTO ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 06 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

LONG V. LE 09/29/07
SUPERVISORY PATENT EXAMINER
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REQUEST FOR RECONSIDERATION

1. Applicants response to the Final Office Action mailed June 6, 2006 is acknowledged (paper filed 9/6/05). Claims 2, 3, 7, and 8 were canceled without prejudice or disclaimer. Currently, claims 1, 4-6, and 9-10 are pending and under consideration.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1, 4, 6, and 9 are rejected under 35 U.S.C.103(a) as being unpatentable over Hunter et al. (Int. Arch. Allergy, 36 354-375, 1969) in view of Dosa et al. (Immunology, 1979, 38, pages 509-517) and further in view of Shinoda et al. (Nippon Ishinkin Gakkai Zasshi, 1991, 32 Suppl.2 Proc. Annu. Meet. Jpn. Soc. Med. Mycol. 34th 1990, pages 83-93).

Hunter et al. teach agglutination procedures to measure antibody-antigen binding. In one embodiment, pepsin treated antibodies are coupled to BSA (protease treated BSA) and use to measure antigen interaction via agglutination. See pepsin of F(ab)2 fragments and 7S on page 356; page 363. Bovine serum albumin (BSA) is proven useful in being coupled to reagents while the reagent binding ability in agglutination procedures is maintained. See page 361 number 2 and table IV.

Hunter et al. are silent with respect to the pepsin digest rendering fragmented BSA. However, Dosa et al. disclose the effect of peptic degradation on the immunological and antigenic properties of bovine serum albumin (BSA). See abstract. BSA was digested with pepsin and the fluorescence-binding efficiency evaluated. The BSA fragments obtained from a digest did not form BSA-anti-BSA immune complexes (see page 511-512) and did not interact with B cells (see page 516, 1st column 1st paragraph). The systematic degradation of BSA with pepsin provided an excellent model for investigating the function and nature of different antigenic determinants present on protein antigens. Page 515, 2nd column – Discussion.

Hunter et al. discloses the claimed invention except for the fragmented BSA produced from pepsin digestion.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to degrade BSA with pepsin thereby producing fragmented BSA because Dosa et al. taught that the systematic degradation of BSA with pepsin provided an excellent model for investigating the function and nature of different antigenic determinants present on protein antigens. Page 515, 2nd column – Discussion.

Hunter et al. in view of Dosa et al. differ from the instant invention in not specifically teaching the utility of latex particles carrying an antibody or antigen specifically reactive with the analyte of interest.

Shinoda et al. teach this limitation. Specifically, Shinoda et al. disclose agglutination tests to measure cryptococcal antigens. The test utilizes a protease treated serum or cerebrospinal fluid sample and a sensitized latex suspension (particles coated with anti-Cryptococcal). The antigen was detectable in soluble immune complexes. The latex assay was sensitive and useful in patient sample evaluations (meningitis, pulmonary cryptococcosis, and cutaneous cryptococcosis). The protease pretreatment of the serum was useful in reducing false positive and false negative results. See abstract.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to use a latex assay as taught by Shinoda et al. in the BSA protease pre-treatment method of Hunter et al. in view of Dosa et al. because Shinoda et al. taught that the latex assay was sensitive and useful in patient sample evaluations (meningitis, pulmonary cryptococcosis, and cutaneous cryptococcosis). Further, the protease pretreatment was useful in reducing false positive and false negative results in the latex assay. See abstract.

II. Claims 5 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al. (Int. Arch. Allergy, 36 354-375, 1969) in view of Dosa et al. (Immunology, 1979, 38, pages 509-517) and further in view of Shinoda et al. (Nippon Ishinkin Gakkai Zasshi, 1991, 32 Suppl.2 Proc. Annu. Meet. Jpn. Soc. Med. Mycol. 34th 1990, pages 83-93) as applied to claims 1, 4, 6, and 9 above, and further in view of Nakase et al. (JP 48019719 Abstract Only).

Please see Hunter et al. in view of Dosa et al. and further in view of Shinoda et al. as set forth above. Hunter et al. in view of Dosa et al. and further in view of Shinoda et al. disclose the reagent combination involving protease treatment in combination with BSA and antigen/antibody coated latex particles. However, Hunter et al. in view of Dosa et al. and further in view of Shinoda et al. do not teach the use of these reagents for anti-streptolysin O antibodies.

Nakase et al. disclose that the addition of BSA (bovine serum albumin) to streptolysin O stabilizes streptolysin O and allows streptolysin O to maintain its activity. See abstract.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the protease treatment in combination with BSA and antigen/antibody coated latex particles detection reagents as taught by Hunter et al. in view of Dosa et al. and further in view of Shinoda et al. and utilize them in turbidity measurements for anti-streptolysin O antibodies/antigen assays because Nakase et al. disclose that the addition of BSA (bovine serum albumin) to streptolysin O stabilizes streptolysin O and allow streptolysin O to maintain its activity. See abstract.

Response to Arguments

3. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., BSA coated latex particles) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In particular, the claims are drawn to a latex particle carrying an antibody or antigen specifically reacting with an antigen or antibody to be assayed. There is not requirement for the antibody or antigen to be BSA or include BSA.

Applicant's contend that the instant invention discovered that internal epitopes embedded within native BSA are not recognized by an anti-BSA antibody (generated against the whole molecule). This argument was carefully considered but not found persuasive because Dosa et al. teach this same discovery. On page 516, 1st column - 1st paragraph stated "The ability of the degraded fragments to form immunoprecipitates with anti-BSA serum was lost early in the course of digestion. The affinity of the peptides for anti-BSA antibody and their efficiency as inhibitors of the BSA-anti-BSA reaction also decreases rapidly."

Applicants also argue that not all antibodies specific to BSA fragments can be absorbed to whole BSA (native) and the elimination of fragmented BSA required specific fragmented antibodies. This argument was carefully considered but not found persuasive because Dosa et al. teach that certain fragments were capable of suppressing the immune response directed towards the native antigen. See page 516, 1st column and 3rd paragraph. In other words, some fragments were not bound by native BSA (whole).

Applicants contend that the combination of references under 35 USC 103 does not teach or suggest the instant invention because the actual teachings of Dosa et al. are drawn to *in vivo* procedures while the claims are drawn to *in vitro* techniques. This argument has been carefully considered but was not found persuasive because Dosa et al. teach *in vitro* procedures to measure fragmented BSA binding.

For example, on page 510 under RESULTS and in figure 1, hydrogen ion uptake and fluorescence-binding efficiency of BSA after various pepsin digestion was evaluated (*in vitro* procedure). On page 511, Immunochemical characterization of the BSA digests were demonstrated *in vitro*. Specifically, digests or fragmented BSA samples were immunoadsorbed onto an anti-BSA sepharose 4B column and fragments digested for longer than 20 minutes were not retained on the anti-BSA column. Haemagglutination inhibition studies were also conducted on the BSA fragments. See page 512 and Table 2.

Further, Applicant contends that Dosa et al. do not teach conventional latex turbidity method. However, Dosa et al. were not cited for convention latex turbidity methods because Shinoda et al. (Nippon Ishinkin Gakkai Zasshi, 1991, 32 Suppl.2 Proc. Annu. Meet. Jpn. Soc. Med. Mycol. 34th 1990, pages 83-93) disclose this limitation. While a deficiency in a reference may overcome a rejection under 35 USC 103, a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

4. For reasons aforementioned, no claims are allowed.

5. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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